REMARKS/ARGUMENTS

This is meant to be a complete response to the Final Office Action mailed April 21, 2006. In the Final Office Action, the Examiner rejected Applicants' claims 1, 6-7, 10, 13, 24-25 and 44-45 under 35 U.S.C. 112, ¶2, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner rejected claims 1, 6-7, 10, 13, 24-25 and 44-45 under 35 U.S.C. 103(a) as being unpatentable over Badylak et al. (US 5,695,998) in view of the two Zhang et al. references (*Pediatrics Journal,* 1999 and *Journal of Urology,* 2000).

Applicants' Response to the 35 U.S.C. 112, ¶2 Rejection

In the Office Action, the Examiner rejected Applicants' claims 1, 6-7, 10, 13, 24-25 and 44-45 under 35 U.S.C. 112, ¶2, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In support of the rejection, the Examiner stated that:

> It is unclear what applicant is claiming in that the claims are drawn to a graft which is SIS seeding with bone marrow stromal cells but wherein the stromal cells have differentiated into smooth muscle cells thus it is unclear if applicant is claiming the stromal cells or the muscle cells.

Applicants respectfully traverse the rejection as applicable to currently pending claims 24, 25, 44 and 45, and newly added claims 56-59.

All of the currently pending claims recite methods for providing a urinary tract tissue graft composition (claims 24, 25, 56 and 57) or methods for repairing a damaged urinary tract tissue of a subject (claims 44, 45, 58 and 59), wherein the methods include the steps of: (1) seeding at least one bone marrow stromal cell on a surface of a segment of small intestinal submucosa; and (2) culturing the composition so formed under conditions such that the at least one bone marrow stromal cell differentiates into a smooth muscle-like cell and exhibits three dimensional growth and matrix penetrance.

Therefore, Applicants are specifically claiming a **method** in which bone marrow stromal cells are seeded, followed by **culturing** so that the cells **differentiate** into smooth muscle-like cells. Thus, the claims require that the cells begin as bone marrow stromal cells and, through the process of the methods of the present invention, differentiate into smooth muscle-like cells.

Applicants respectfully submit that currently pending claims 24, 25, 44 and 45, as well as newly added claims 56-59 which depend therefrom, are definite and particularly point out and distinctly claim that which Applicants regard as the invention. Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 112, ¶2 rejection of the pending claims.

Applicants' Response to the 35 U.S.C. 103(a) Rejection

In the Office Action, the Examiner rejected claims 1, 6-7, 10, 13, 24-25 and 44-45 under 35 U.S.C. 103(a) as being unpatentable over Badylak et al. (US 5,695,998) in view of the two Zhang et al. references (*Pediatrics Journal,* 1999 and *Journal of Urology,* 2000). Applicants respectfully traverse the rejection for the reasons stated hereinbelow.

Currently pending claims 24, 25, 44 and 45 of the subject application (as well as newly added claims 56-59 which depend therefrom), recite methods for providing a urinary tract tissue graft composition (claims 24, 25, 56 and 57) or methods for repairing a damaged urinary tract tissue of a subject (claims 44, 45, 58 and 59). Each method includes the steps of: (1) seeding at least one bone marrow stromal cell on a surface of a segment of small intestinal submucosa; and (2) culturing the composition so formed under conditions such that the **at least one bone marrow stromal cell *differentiates* into a smooth muscle-like cell and exhibits *three dimensional growth* and *matrix penetrance***. Claims 44, 45, 58 and 59 recite the additional step of contacting damaged urinary tract tissue with the seeded segment of small intestinal submucosa to repair the damaged urinary tract tissue and restore urological function.

Badylak et al. teach a cell culture growth substrate comprising submucosal tissue having eukaryotic cells contacted thereto. Badylak et al.

teach growing a variety of **unipotent** cell types on submucosal tissue. While Badylak et al. briefly mention seeding mesenchymal cells on the submucosal tissue at Column 6, lines 34-36, Badylak et al. simply teach **expansion** of this cell population on the submucosal tissue and ***NOT DIFFERENTIATION*** of the mesenchymal cells into another cell type on the submucosal tissue. Further, Badylak et al. simply suggest that mesenchymal cells could be seeded on submucosal tissue, but Badylak et al. ***DO NOT DEMONSTRATE*** that mesenchymal cells will actually grow on submucosal tissue, and therefore Badylak et al. ***DO NOT ENABLE*** a teaching of seeding mesenchymal cells on submucosal tissue.

In the Office Action, the Examiner asserts that Badylak et al. "discusses that **stem cells** can be proliferated, expanded and/or **differentiated** on the graft" (Office Action, Page 3, lines 2-3 of the last paragraph, emphasis added). However, the only reference in Badylak et al. to differentiation is found in Example 5. The **"cytodifferentiation"** of Example 5 refers to **unipotent**, **fetal** epithelial cells differentiating into adult epithelial cells by the natural epithelial cell maturation process. This is not the same as, nor similar to, the differentiation of a **multipotent** cell into a different cell type. The bone marrow stromal cells recited in the claims of the subject application are multipotent cells that can differentiate into a variety of cell types, as opposed to the epithelial cells taught by Badylak et al., which can only differentiate from fetal cells into

adult cells, and cannot differentiate into a different cell type. Badylak et al. do not teach, disclose or even suggest differentiation of a multipotent cell into a different cell type on submucosal tissue, as Badylak et al. only teach expansion, maturation and proliferation of unipotent cells on submucosal tissue. Thus, Badylak et al. do not enable a cell culture growth substrate comprising submucosa and stem cells, as the Examiner has asserted.

The presently claimed invention is the first demonstration of differentiation of a multipotent cell into another cell type on submucosal tissue.

In addition, Badylak et al. do not teach, disclose or even suggest growing urinary tract cells on submucosal tissue, nor do Badylak et al. teach, disclose or even suggest methods of providing a urinary tract tissue graft composition or repairing a damaged urinary tract tissue, nor do Badylak et al. teach seeding a multipotent cell on submucosal tissue such that the multipotent cell differentiates into a urinary tract cell type.

The Examiner has recognized the deficiencies of Badylak et al. and has attempted to supply such deficiencies with the teachings of the two Zhang et al. references.

Zhang et al. (*Journal of Urology*, 2000) was published in September 2000, and the effective filing date of the subject application is December 8, 2000. Since this publication is within one year of the effective filing date of the

subject application and is a publication of the inventor's own work, it is not available as prior art under 35 U.S.C. 102/103. A Declaration under 37 C.F.R. § 1.132 disqualifying this reference as prior art is filed herewith. Therefore, Applicants respectfully submit that Zhang et al. (*Journal of Urology*, 2000) is not a proper reference under 35 U.S.C. 103(a).

Zhang et al. (Pediatrics Journal, 1999) disclose the co-culture of bladder urothelial and smooth muscle cells on small intestinal submucosa; however, this reference doe not teach, disclose or even suggest the use of bone marrow stromal cells, nor does this reference teach, disclose or suggest the differentiation of a multipotent cell (i.e., bone marrow stromal cell) into another cell type (i.e., smooth muscle-like cell) while seeded on small intestinal submucosa. Thus, this reference adds nothing to the fact that the primary reference of Badylak et al. does not teach, disclose or even suggest the inventive concept recited in the pending claims.

Further, a person of ordinary skill in the art would not find motivation nor suggestion in the combination of Badylak et al. and Zhang et al. to seed a multipotent cell (i.e., a bone marrow stromal cell) on a segment of small intestinal submucosa for differentiation of the multipotent cell into another cell type, and the combination of references does not teach, disclose or even suggest a method involving differentiation of a multipotent cell into a different cell type.

Applicants respectfully submit that pending claims 24, 25, 44 and 45 of the subject application (as well as newly added claims 56-59 which depend therefrom) are non-obvious over Badylak et al. in view of Zhang et al. Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 103(a) rejection of the claims as now pending.

CONCLUSION

This is meant to be a complete response to the Final Office Action mailed April 21, 2006. Applicants respectfully submit that each and every rejection of the claims, as now pending, has been overcome. Further, Applicants respectfully submit that currently pending claims 24, 25, 44 and 45, as well as newly added claims 56-59, are patentable over the art of record and are in a condition for allowance. Favorable action is respectfully solicited.

Should the Examiner have any questions regarding this Amendment, or the remarks contained herein, Applicants' agent would welcome the opportunity to discuss such matters with the Examiner.

Respectfully submitted,

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